IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re application of | : | **Confirmation No. 3187** |
| Shinichiro ISOBE | : | Atty Docket No. 2004_0569A |
| Serial No. 10/822,775 | : | Group Art Unit 1645 |
| Filed April 13, 2004 | : | Examiner Unassigned |
| METHOD OF DETECTING BIOLOGICAL MOLECULES, AND LABELING DYE AND LABELING KIT USED FOR THE SAME | : | Mail Stop: PETITION |

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

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Respectfully submitted,

Shinichiro ISOBE

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May 17, 2005

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**PETITION TO MAKE SPECIAL UNDER 37 C.F.R. § 1.102(d)**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

Sir:

Applicant requests that the above-identified application be granted special status in accordance with M.P.E.P. § 708.02 (VIII). In addition to the required remarks which follow, the required fee as set forth in 37 C.F.R. § 1.17(h) accompanies this petition.

Original claims 1-20 have been canceled and replaced by new claims 21-32 by way of the Preliminary Amendment filed concurrently herewith.

Claims 21-32, including independent claims 21, 25, 27 and 30, are presently pending in this application. Applicant submits that claims 21-32 are all directed to a single invention.

The required pre-examination prior art search has been performed. In particular, a Boolean online computer search at the USPTO website was conducted.

The classes and sub-classes searched include: 428/690; 428/917; 428/704; 548/416; 548/452; 548/453; 313/504; 313/506 and 435/28.

The following keyword terms were searched: labeling dye AND (thiazole, oxazole, azole OR imidazole derivat$); thiazole derivat$ AND (labels or labeling dyes); oxazole derivat$ AND (labels or labeling dyes); azole derivat$ AND (labels or labeling dyes); imidazole derivat$ AND (labels or labeling dyes); diazole derivat$ AND (labels or labeling dyes); organic

electroluminescence (EL) dyes, EL-dyes AND (labels or labeling dyes); mono-azole derivat$; triazole derivat$; oxazolopyridine; thiophene derivat$; and oxadiazole derivat$.

The references found during this pre-examination search which are deemed most closely related to the subject matter encompassed by the claims are:

1. Okada et al., US 6,551,723;
2. Okada et al., US 6,461,747;
3. Okada et al., US 6,656,612 (divisional to US 6,461,747);
4. Okada et al., US 6,830,836 (divisional to US 6,656,612 and US 6,461,747);
5. Okada et al., US 6,824,891;
6. Okada, US 6,528,187;
7. Igarashi et al., US 6,358,634;
8. Yamada et al., US 6,696,182;
9. Taguchi, US 6,461,538;
10. Taguchi, US 6,673,928 (divisional to US 6,461,538);
11. Taguchi, US 6,451,457;
12. Oyama et al., US 5,206,149; and
13. Suzuki et al., US 5,856,479

Each of these references is being cited and a copy of each is being submitted concurrently herewith in an Information Disclosure Statement.

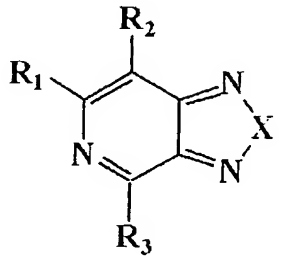
Applicant respectfully submits that the subject matter recited in the claims is patentable over each of these references for the reasons discussed below.

The organic labeling dye according to the present invention is characterized in that it is a labeling dye used for detecting a biological molecule by measurement of fluorescence. The labeling dye comprises an organic EL-dye having a reactive group that binds to a biological molecule.

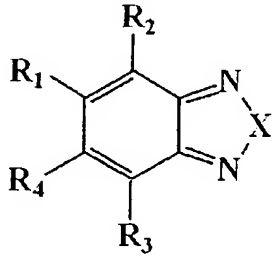
Claims 21-32 require an organic EL-dye limited to the specific compounds described in the specification.

Specifically, independent claim 21 is directed to a method of detecting a biological molecule comprising reacting a sample containing a biological molecule with an organic EL-dye, and measuring the fluorescence of the biological molecule labeled with the organic EL-dye. Independent claim 27 is directed to the organic EL-dye itself, and independent claim 30 is

directed to a kit thereto. The organic EL-dyes of claims 21, 27 and 30 are the specific compounds selected from the group consisting of the following formula (1) to (6):



(1)



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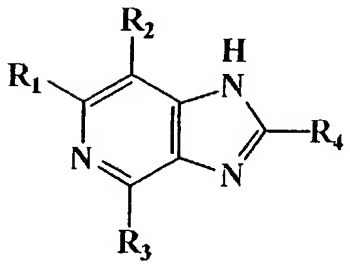
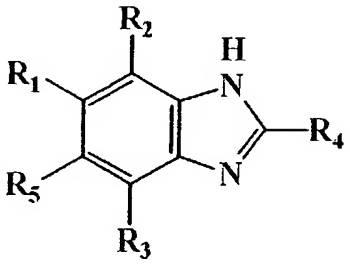


(3)



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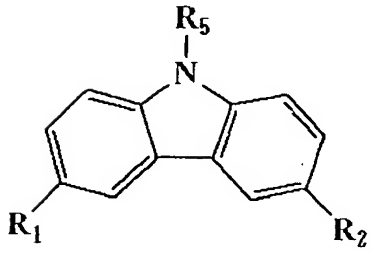

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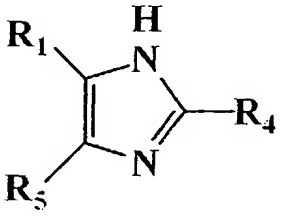
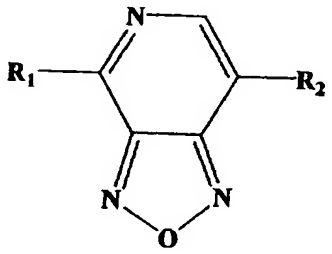


(6)

wherein, $R_1$, $R_2$, $R_3$, $R_4$ and $R_5$ are each independently an aromatic hydrocarbon group, hydrocarbon group, heterocyclic group or aromatic group containing a hetero atom in the ring, optionally having a substituent selected from hydrogen atom, halogen atom, hydroxyl group, cyano group or sulfonyl group, and X is a nitrogen atom, sulfur atom, oxygen atom, selenium atom or boron atom, optionally having a substituent.

Independent claim 25 is directed to a method of detecting a biological molecule comprising reacting a sample containing the biological molecule with a labeling dye comprising an oxazolopyridine derivative, to label the biological molecule, and measuring the fluorescence of the labeled biological molecule in the sample, wherein the oxazolopyridine derivative is a compound of the following formula:




wherein, $R_1$ and $R_2$ are each independently an aromatic hydrocarbon group, hydrocarbon group, heterocyclic group or aromatic group containing a hetero atom in the ring, optionally having a substituent selected from hydrogen atom, halogen atom, hydroxyl group, cyano group or sulfonyl group.

The present invention has the following advantages and effects, which not present in the dyes of the prior art.

The organic EL-dye of the present invention shows high quantum yield in solid state (including solid state and semi-solid state). Thus, the present invention manifests high fluorescence intensity.

The organic EL-dye of the present invention is also relatively inexpensive, especially when compared with conventional fluorescence dyes, such as Cy3 and Cy5. Accordingly, use of the present invention allows the detection of biological molecules at lower cost.

Further, the organic EL-dye of the present invention reacts with a biological molecule almost quantitatively and shows a high incorporation ratio. This results in a high detection sensitivity.

Furthermore, the use of the organic EL-dye of the present invention increases the degree of freedom of selectivity of fluorescence wavelength. Also, multiple fluorescence wavelengths

of orange, yellow, green, blue can be used. Accordingly, it becomes possible to use two or more fluorescence dyes having a large stokes shift (i.e., large difference between excited wavelength and fluorescence wavelength). Consequently, plural target biological molecules, such as nucleic acids, contained in one sample can also be simultaneously detected.

Also, while prior art dyes, such as Cy3 and Cy5, need to be kept in refrigerated state, the organic EL-dye of the present invention is chemically stable and can be kept for a long time at ambient temperature. Thus, handling of the organic EL-dye of the present invention is easier.

Applicant respectfully submits that the organic EL-dyes of the claimed invention are neither disclosed nor suggested by References 1 to 13 from the pre-examination search.

**Reference 1 -- Okada et al., US 6,551,723**

The invention of US '723 relates to a light-emitting organic EL element material, which can convert electric energy to light to emit light and a light-emitting (luminescent) element comprising such. The organic EL element material is a heterocyclic compound in which a 5- or 6-membered ring is condensed with a 5- to 7-membered ring. (Column 2, lines 35-40). Specific examples of the 5- or 6- membered rings constituting the condensed ring include furane, thiophene, pyran, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, thiazole, oxazole, isothiazole, isoxazole, thiadiazole, oxadiazole, triazole, pyrroline, imidazoline, pyrazoline, and triazine. (Column 5, lines 12-24; column 8, line 35 to column 9, line 25; Column 8, lines 25+).

**References 2-4 -- Okada et al., US 6,461,747, US 6,656,612 & US 6,830,836**

The disclosures of US '747, US '612 and US '826 relate to a material for a light emitting device, which consists of a compound containing monocyclic or condensed ring type heterocyclic groups (each having preferably 1 to 20 carbon atoms, more preferably 1 to 12 carbon atoms, and still more preferably 2 to 10 carbon atoms), and preferably aromatic heterocyclic groups each containing at least one of nitrogen, oxygen, sulfur and selenium atoms. (See Abstract and column 14, lines 1-65 in US '747; and Formulae (I) and (III) at these locations). Examples of the heterocyclic group include pyrrolidine, piperidine, pyrrole, furan, thiophene, imidazoline, imidazole, benzimidazole, naphthimidazole, thiazolidine, thiazole, benzthiazole, naphthothiazole, isothiazole, oxazoline, oxazole, benzoxazole, naphthoxazole, isoxazole, selenazole, benzoselenazole, naphthoselenazole, pyridine, quinoline, isoquinoline, indole, indolenine, pyrazole, pyrazine, pyrimidine, pyridazine, triazine, indazole, purine, phthalazine,

naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, phenanthridine, phenanthroline and tetraazaindene. (See formulae III and IV at column 2, line 56 to column 3, line 35 and column 14, lines 1-65 in US '747).

**Reference 5 -- Okada et al., US 6,824,891**

The disclosure of US '891 relates to a light-emitting device comprising a pair of electrodes formed on a substrate, and organic compound layers comprising a light-emitting layer provided in between the electrodes, wherein at least one of the organic compound layers comprises a heterocyclic compound having at least two hetero atoms and a phosphorescent compound. (Abstract; column 1, line 48 to column, 2, line 16, Formula (I); column 7, lines 55-65, Formula (II)). The heterocyclic group is a monocyclic or condensed heterocyclic group which preferably contains 1 to 20, particularly 1 to 12, especially 2 to 10, carbon atoms, preferably an aromatic heterocyclic group having at least one of a nitrogen atom, an oxygen atom, a sulfur atom and a selenium atom. Examples of the heterocyclic compounds include pyrrolidine, piperidine, piperazine, morpholine, thiophene, selenophene, furan, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyridazine, pyrimidine, triazole, triazine, indole, indazole, purine, thiazoline, thiazole, thiadiazole, oxazoline, oxazole, oxadiazole, quinoline, isoquinoline, phthalazine, naphthyridene, quinoxaline, quinazoline, cinnoline, pteridine, acridine, phenanthroline, phenazine, tetrazole, benzimidazole, benzoxazole, benzothiazole, benzotriazole, tetraazaindene, carbazole, and azepin. (Column 6, line 54 to column 7, line 6).

**Reference 6 -- Okada, US 6,528,187**

The disclosure of US '187 relates to a luminescence element comprising a compound containing an atomic group necessary to form a 5- or 6-membered nitrogen-containing aromatic heterocyclic ring. Examples of 5- or 6-membered nitrogen-containing aromatic heterocyclic ring include pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, thiazole, isothiazole, oxazole, isoxazole, selenazole, and triazine, preferably pyridine, pyrazine, pyrimidine, and pyridazine, more preferably pyridine and pyrazine, and particularly preferably pyridine. (See Abstract; column 7, lines 1-15).

**Reference 7 -- Igarashi et al., US 6,358,634**

The disclosure of US '634 relates to an organic light-emitting device material, such as electron-transporting material and light-emitting material comprising a compound containing a 5- or 6-membered aromatic ring. Examples of the ring include cyclopentene, cyclohexene, benzene,

naphthalene, anthracene, phenanthrene, pyrene, perylene, pyridine, quinoline, furan, thiophene, pyrazine, pyrimidine, thiazole, benzothiazole, naphthothiazole, oxazole, benzoxaole, naphthoxazole, isoxazole, selenazole, benzoselenazole, naphthoselenazole, imidazole, benzoimidazole, naphthoimidazole, isoquinoline, pyrazole, and triazole. (Column 6, lines 12-19). Preferred examples of the aromatic ring include benzene, naphthalene, anthracene, pyridine, thiophene, pyrazine, and pyrimidine. (Column 5, lines 21-23).

**Reference 8 – Yamada et al., US 6,696,182**

The disclosure of US '182 relates to an organic EL device comprising thiophene derivatives, in particular, dipyridylthiophene derivatives. (Abstract; column 2, lines 45-68; and column 4, line 15 to column 5, line 16). US '182 indicates that there are no particular restrictions on the other electron transport materials to be used in the organic EL device, and such materials include those that are commonly used in the prior art as electron transferring compounds for photoconductive materials, or any publicly known materials used in electron injection layers and electron transport layers of organic EL devices. Examples of such electron transferring compounds include: diphenylquinone derivatives (those described in Journal of the Society of Electrophotography of Japan, 30(3), 266 (1991), etc.), perylene derivatives (those described in J. Appl. Phys., 27, 269 (1988), etc.), oxadiazole derivatives (those described in Jpn. J. Appl. Phys., 27, L713 (1988), Appl. Phys. Lett., 55, 1489 (1989), etc.), thiophene derivatives (those described in JP-A 4-212286, etc.), triazole derivatives (those described in Jpn. J. Appl. Phys., 32, L917 (1993), etc.), thiadiazole derivatives (those described in Polymer Preprints, Japan, 43, (III), Pla007, etc.), metal complexes of oxine derivatives (those described in Technical Report of the Institute of Electronics, Information and Communication Engineers, 92(311), 43 (1992), etc.), polymers of quinoxaline derivatives (those described in Jpn. J. Appl. Phys., 33, L250(1994), etc.), phenanthroline derivatives (those described in Polymer Preprints, Japan, 43, 14J07, etc.) and silacyclopentadiene derivatives (those described in JP-A 9-87616, etc.). (Column 6, lines 37-62).

**References 9-10 -- Taguchi, US 6,461,538 & US 6,673,928**

The disclosures of US '538 and US '928 relate to an organic light-emitting device comprising a compound containing a light-emitting layer comprising an amine compound and/or other light-emitting materials. The light-emitting materials include various metal complexes and orthometalated complexes including metal complexes and rare earth complexes of benzoxazole

derivative, benzimidazole derivative, benzothiazole derivative, styrylbenzene derivative, polyphenyl derivative, diphenylbutadiene derivative, tetraphenylbutadiene derivative, naphthalamide derivative, coumarin derivative, perylene derivative, perynone derivative, oxadiazole derivative, aldazine derivative, pyralidine derivative, cyclopentadiene derivative, bisstyrylanthracene derivative, quinacridone derivative, pyrrolopyridine derivative, thiazolopyridine derivative, cyclopentadiene derivative, styrylamine derivative, aromatic dimethylidyne compound and 8-quinolinol derivative, and polymer compounds such as polythiophene, polyphenylene and polyphenylenevinylene. (Column 34, lines 18-40).

**Reference 11 – Taguchi, US 6,451,457**

The disclosure of US '457 relates to an organic luminous material, which comprises a 1,2,4-oxadiazole compound derivative. (Abstract: column 2, lines 11-12).

**Reference 12 -- Oyama et al., US 5,206,149**

The disclosure of US '149 relates to a method for detecting the presence of a substance by the chemiluminescence using oxazole derivatives. (Abstract; column 2, lines 12-35). It is indicated that such method is useful for the detection of genes in a microorganism. (Column 1, lines 59-60).

**Reference 13 -- Suzuki et al., US 5,856,479**

The disclosure of US '479 relates to a chemiluminescence method for detecting the biological substance, such as nucleic acid, using a fluorescent group-containing carbodiimide compound, wherein the flourescent moiety includes a coumarin derivative, a pyrene derivative, a perylene derivative, a rhodamine derivative, a dansyl derivative, an oxazole derivative, a thiazole orange derivative, and the like. (Column 5, lines 1-20; column 15, lines 50-55). It is indicated that the fluorescence intensity is increased by binding or intercalating to DNA or RNA, the fluorescence material for example, thiazole orange derivative. (Column 5, lines 1-20).

Again, the new claims require an organic EL-dye limited to the specific compounds described in the specification as noted above.

Applicant respectfully submits that the above-cited References 1-13 do not disclose or suggest the organic EL-dyes of new independent claims 21, 25, 27 and 30 or the claims depending therefrom.

In view of the above, it is respectfully submitted that the Applicant has complied with the requirements of M.P.E.P. § 708.02 (VIII). Accordingly, this Petition under 37 C.F.R. § 1.102(d) should be granted.

Favorable action on the merits is now solicited.

Respectfully submitted,

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